Guidance for Industry
Indexing
Structured Product Labeling

DRAFT GUIDANCE

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U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

March 2007
Electronic Submissions

Contains Nonbinding Recommendations
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Guidance for Industry
Indexing
Structured Product Labeling

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Guidance for Industry[1]
Indexing Structured Product Labeling

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I. INTRODUCTION

This guidance explains that FDA's Center for Drug Evaluation and Research (CDER), rather than industry, will index SPL (Structured Product Labeling) in product labeling for human drugs. (Indexing refers to the insertion of machine readable tags, which do not appear in actual printed labeling, to allow users to rapidly search and sort product information.) This guidance also makes recommendations on how to request a change to the indexing information in SPL. Having consistently and accurately indexed SPL is an important step toward the creation of a fully automated health information exchange system.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

A. When Did the Use of SPL Become a Requirement?

Since October 31, 2005, labeling submissions to CDER must be in SPL format (see 21 CFR 314.50(l)(1)(i) and (l)(5) and 314.71(b); see also Memorandum 32 to Docket Number 92S-0251). In addition, annual report submissions must contain content of labeling in SPL format (see 21

[1] This guidance has been prepared by the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration.

CFR 314.81(b)(2)(iii)) (note, however, that applicants should not submit SPL with an annual report if there are no changes to the previously submitted SPL).[2]

An Health Level Seven (HL7)[3] standard, SPL is used for electronically exchanging the content of labeling and other regulated product information using the extensible markup language (XML). SPL is also a key component of Facts@FDA,[4] which makes regulated product information in SPL publicly available through the National Library of Medicine's DailyMed Web site and on FDA's Web page.[5]

B. Why Is Indexing SPL So Important?

Indexing the SPL will greatly enhance users' ability to automatically search and sort product information. The American healthcare community (e.g., federal healthcare agencies, healthcare providers, healthcare professionals, industry) is working toward the creation of a fully automated health information system. Eventually, patients and healthcare professionals and providers will have electronic health records, electronic prescribing systems, and an array of clinical decision support systems and tools at their disposal. Being able to electronically access labeling information and search and sort that information is an important step toward the creation of a fully automated health information exchange system.

Health information suppliers take the information from the content of product labeling to populate databases that are used in clinics and hospitals to help prevent prescribing errors. In the past, much of this information was input by hand. Since October 31, 2005, FDA has been making that information available for prescription drugs free of charge on the Internet through the use of SPL. Currently, the only way to search the labeling that is available in SPL format is using full-text search, which has obvious limitations. For example, if a user searches for "hepatotoxicity," she will miss labels that use the term "liver toxicity." Addition of indexing elements based on standard terminology will address this problem. Once FDA has indexed the labeling in SPL, the prescription drug information that FDA has made available on the Internet, will be much more useful, because the indexing elements will enhance user ability to quickly access, search, and analyze the labeling information needed to make critical healthcare decisions.

Having consistently and accurately indexed SPL will also greatly enhance the safe use of medical products. In July 2006, the Institute of Medicine of the National Academy of Sciences estimated that more than 1.5 million people annually are injured due to medication errors. The cost of treating hospital-based medication errors alone is conservatively estimated at more than $3.5 billion annually, and this cost does not even include estimates for lost wages and lost productivity.[6] One source of many of these errors is prescribing errors, which can result in

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[2] See FDA guidance for industry *SPL Standard for Content of Labeling Technical Qs & As* question #41.

[3] See http://www.hl7.org.

[4] See http://www.fda.gov/oc/datacouncil/drug_labels.htm.

[5] See http://dailymed.nlm.nih.gov/dailymed/about.cfm and http://www.fda.gov/oc/datacouncil/drug_labels.htm

[6] See http://www8.nationalacademies.org/onpinews/newsitem.aspx?RecordID=11623.

avoidable adverse drug reactions. For example, if a patient with asthma is taken to the hospital in an emergency situation for an unrelated physical injury, the SPL indexing elements would enable the hospital to use its computer system to quickly identify all drugs contraindicated in patients with asthma and treat the patient accordingly. Among other benefits, the SPL indexing elements could also enable the hospital's computer system to ensure that medications prescribed by the hospital to treat the patient's injury do not adversely interact with other medications that the patient takes to treat her asthma. In short, the SPL indexing elements, when coupled with other computer technologies, will provide patients and healthcare providers with better and ***more timely*** access to important healthcare information.

Finally, indexing SPL directly supports FDA's mission because this effort will help Americans "get the accurate, science-based information they need to use medicines…to improve their health."[7] Indexing also addresses a recommendation in the Institute of Medicine's 2006 report on drug safety, which identified the need for improved communication between FDA and the public about drug safety and efficacy information.[8] Indexing elements will greatly facilitate this communication, helping create a more robust nationwide system for promoting the safe and effective use of drugs.

III. FDA'S STRATEGY FOR INDEXING SPL

A. Why Is FDA Indexing SPL?

The SPL standard enables the inclusion of *indexing elements*, which are machine-readable tags that can be added to product labeling to enable users to rapidly search and sort product information. For example, the pharmacologic class indexing element for a monoamine oxidase inhibitor is associated with the preferred term "monoamine oxidase inhibitors" and the associated code (N0000000184) from the Veterans Administration National Drug File Reference Terminology (NDF-RT).[9] FDA would index a monoamine oxidase inhibitor as follows:

```
<generalizedPharmaceuticalClass>
    <code code="N0000000184" codeSystem="2.16.840.1.113883.3.26.1.5" displayName="monoamine oxidase inhibitors"/>
</generalizedPharmaceuticalClass>
```

[7] See FDA Mission Statement at http://www.fda.gov/opacom/morechoices/mission.html.

[8] See "The Future of Drug Safety: Promoting and Protecting the Health of the Public" at http://www.iom.edu/CMS/3793/26341/37329.aspx.

[9] NDF-RT includes the controlled terminology for mechanism of action, physiologic effect, and structural class, which are part of the Federal Medication Terminology standard.

Because indexing serves only to electronically flag or identify information of a particular type, indexed elements are not visible in the printed labeling. However, these flags can be used to sort and categorize the information so that it will be more readily accessible in electronic systems. It is important that this indexing be done consistently because if different approaches are used to determine what the appropriate flag is or where it should be placed, eventual searches of indexed SPL labeling will be less comprehensive and may not turn up all relevant information, which could have significant health consequences.

FDA has been piloting the addition of indexing elements to SPL in labeling that has been submitted consistent with the new content and format regulation for prescription drug labeling.[10] Although a number of different approaches were tried during the pilot program, based on our experience and feedback from industry and other SPL users, we have determined that the most efficient strategy is for FDA, ***not individual applicants***, to index the information in SPL. Having FDA insert the indexing elements in SPL will further the goal of efficiency and consistency, eliminating possible intercoder variability that could occur if individual sponsors were responsible for determining the placement of the specific indexing flags.

B. How will FDA Index SPL?

Elements used to index SPL will be chosen from standards adopted for use in the healthcare setting. For drug products, indexing information includes, among other things, the indication, limitations of use, conditions of use, and pharmacologic class of the drug. Once FDA has indexed the product labeling, health information suppliers can package indexed information about a product and make it available to healthcare professionals and others through health information systems, such as clinical decision support tools and electronic prescribing systems. More information on SPL, including all SPL indexing elements and their related terminologies, is available at the FDA Data Standards Council Web site.[11]

FDA plans to index SPL using a phased implementation. In the first phase, we plan to add a few key index elements to all labels. In each of the following phases, FDA will add a few more elements to all SPL labels until all of the indexing elements have been added to all labels.[12] This phased implementation will help maximize the utility of the indexing elements given available resources.

Generally, FDA will select the appropriate information for indexing, based on the content of labeling and the selected terminologies.[13] To make the process as transparent as possible, FDA

[10] See http://www.fda.gov/cder/regulatory/physLabel/default.htm.

[11] See http://www.fda.gov/oc/datacouncil/spl.html (Note: the SPL Implementation guide refers to indexing elements as highlights data elements. These terms are synonymous).

[12] Another approach we considered involved adding all indexing elements to a small number of labels using a phased approach. But, given available resources, we decided it would be more useful to add a few indexing elements to all labels. That way, all labels will contain certain key indexing elements.

[13] If an appropriate term is not available in an existing terminology, FDA will work with the relevant terminology maintenance organizations to identify a new term.

will list on the SPL Web page[14] the terminologies and the specific elements it plans to use to index the SPL for all labels.[15] FDA will solicit public input from SPL users through public meetings and announcements in the *Federal Register* on new indexing elements and terminology.

FDA plans to index the pharmacologic class for all labels in SPL as a first step. We are adding pharmacologic class first because (1) it is important for the safe use of drugs, (2) it is necessary for making future indexing meaningful (e.g., drug interactions), and (3) this choice leverages existing FDA resources. After pharmacologic class, we will decide which indexing elements should be added in future phases.

IV. REVISING/CHANGING AN INDEXING ELEMENT

Because FDA will be indexing the SPL, applicants should not add indexing elements to new, or change indexing elements in, existing SPL.

We recommend that applicants submit any questions regarding an existing indexing element, including any requests to add or revise an element to spl@fda.hhs.gov. Inquiries and requests will be forwarded to the appropriate FDA personnel who will consider them and make the appropriate change in the SPL.

Disagreements that cannot be resolved at this level should be handled according to procedures outlined in the guidance for industry *Formal Dispute Resolution: Appeals Above the Division Level*.

[14] See http://www.fda.gov/oc/datacouncil/spl.html.

[15] The timing of subsequent phases will depend on available FDA resources.